

### **REMARKS**

Further to the final Office Action of November 10, 2011, and the Advisory Action issued on February 28, 2011, the present amendments, remarks and associated Declaration are submitted pursuant to 37 C.F.R. §1.114.

#### **Status of the claims**

Claims 1-2 and 4-8 are pending in the application. Claims 5 and 7 are withdrawn. Claim 1 has been amended herein to define the retinoid as specifically being retinal. No new matter has been added with the amendment to claim 1. As such, entry and consideration thereof are respectfully requested.

#### **Rejection under 35 U.S.C. §103**

The instant invention, as encompassed by claim 1, is drawn to topical compositions, comprising as an active ingredient, one or more hyaluronate fragments, wherein the hyaluronate fragments all have a molecular weight of between 50,000 and 750,000 Da and retinal. The Examiner rejects the claims as being obvious over the combined teachings of Liu et al. combined with Balazs.

Applicants traverse the rejection and withdrawal thereof is respectfully requested. Attached hereto is a Declaration of Inventor Dr. Jean-Hilaire SAURAT, which is submitted under 37 C.F.R. §1.32. Also submitted with the Declaration is the journal article of Barnes et al., "Synergistic Effect of Hyaluronate Fragments in Retinaldehyde-Induced Skin Hyperplasia Which Cd44-Dependent Phenomenon" PLoS one, 5(12):e14372 (December 16, 2010), of which Dr. SAURAT is a coauthor.

Dr. SAURAT discusses in the Declaration that the experiments described in the Barnes et al. article, in part, considered the effects of retinal (RAL) + hyaluronate fragments (HAF) on keratinocyte proliferation. Dr. SAURAT further states that "It is known that keratinocyte proliferation is related to therapeutic efficacy in treating dermatoporosis" and that "One skilled in the art would, therefore, consider an activity of inducing keratinocyte proliferation to be predictive of an efficacy for improving wrinkles and dry skin. Indeed previous publications

where the same screening keratinocyte proliferation assays were used, included the demonstration of efficacy in dermatoporosis even in human skin (Kaya et al PLoS Med 2006).”

The data presented in Figure 1 A of Barnes et al. show that RAL combined with HAF provided synergistic activity for stimulating keratinocyte proliferation. The activity seen with RAL and HAF is much higher than with other retinoids, including retinol, retinoic acid or retinoyl palmitate. The data of Figure 1A, therefore demonstrate an unexpected improved activity seen with the specific combination of HAF and RAL that is not seen with other retinoid compounds when combined with RAL.

Dr. SAURAT further states that “The experiments described in the Barnes et al. article were performed with hyaluronate fragments of medium size (50 000 - 400 000 Da). The experiments with hyaluronate fragments of 50 000 - 750 000 Da should certainly reveal similar results. Indeed, hyaluronate fragments of 400 000 - 750 000 Da contain also effective fragments.”

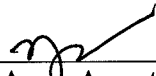
As such, the presently claimed invention possesses unexpected improved properties, which are in no way suggested by Liu et al. or Balazs. The present invention is therefore not obvious over the reference teachings and withdrawal of the rejection is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD, Registration No. 40069, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: May 10, 2011

Respectfully submitted,

By   
MaryAnne Armstrong, PhD  
Registration No.: 40069  
BIRCH, STEWART, KOLASCH & BIRCH, LLP  
8110 Gatehouse Road, Suite 100 East  
P.O. Box 747  
Falls Church, VA 22040-0747  
703-205-8000

Attachment(s)